

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE



Appellants: Raymond J. Dattwyler, Gerald Seinost, Daniel Dykhuizen, Benjamin J. Luft and Maria J.C. Gomes-Solecki

Application No.: 09/596,746 Group: 1645

June 19, 2000 Examiner: R.P. Swartz

Confirmation No.: 3998

For: GROUPS OF *BORRELIA BURGDORFERI* AND *BORRELIA AFZELLI*
THAT CAUSE LYME DISEASE IN HUMANS

CERTIFICATE OF MAILING	
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APPEAL BRIEF

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Commissioner for Patents
P.O. Box 1450
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Sir:

This Appeal Brief is submitted pursuant to the Notice of Appeal received in the U.S. Patent and Trademark Office on August 12, 2004, and in support of the appeal from the final rejections set forth in the Office Action mailed on February 10, 2004. The fee for filing a brief in support of an appeal is enclosed. A Petition for Extension of Time and the appropriate fee are being filed concurrently.

I. REAL PARTY IN INTEREST

The real parties in interest are Brook Biotechnologies, Inc., Long Island High Technology Incubator, 25 East Loop Road, Suite 126, Stony Brook, New York; Research Foundation of the

State University of New York, N5002 Melville Library, Stony Brook, New York; and Baxter BioScience, One Baxter Way, Westlake Village, CA, licensee of the subject matter described in the subject application. Brook Biotechnologies, Inc., and Research Foundation of the State University of New York are the Assignees of the entire right, title and interest in the subject application, by virtue of an Assignment recorded on November 27, 2000 at Reel 011331, Frames 0265-0268 and 0052-0058, respectively.

II. RELATED APPEALS AND INTERFERENCES

Appellants, the undersigned Attorney, Assignees and Licensee are not aware of any related appeals or interferences which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

III. STATUS OF CLAIMS

Claims 1-48 were pending prior to the amendment after final. Claims 1-13, 39 and 41-43 were finally rejected and Claims 14-38 and 44-48 were withdrawn from consideration. In an Amendment After Final (AAF), received by the U.S. Patent and Trademark Office on June 10, 2004, Claims 1-6 were amended, Claims 12-38 and 44-48 were canceled, and Claims 49-52 were added as described below. An Advisory Action has not been prepared or received by Applicants' Attorney as of February 7, 2005. However, the claims as they would appear upon entry of the AAF are presented in the attached Claims Appendix. Claims 1-11, 39, 41-43 and 49-52 are appealed.

IV. STATUS OF AMENDMENTS

Applicants' Attorney filed an Amendment After Final Rejection (AAF) under 37 C.F.R. § 1.116 by facsimile with the U.S. Patent and Trademark Office (USPTO) on June 10, 2004. According to Patent Application Information Retrieval at the USPTO, the Amendment After Final was received on June 10, 2004 and the file was forwarded to the Examiner on August 30, 2004. The Amendment After Final included the amendments that the Examiner stated would overcome the sole rejection in telephonic interviews with the Applicants' Attorney on May 25,

2004. The status of the Amendment After Final is believed to be received, but not acted upon by the Examiner.

In preparation for the scheduled a telephonic interview, Applicants' Attorney provided a draft set of claims canceling Claims 12-38 and 44-48, amending Claims 1-6 to remove the phrase "immunogenic fragments thereof," further amending Claim 1 to remove item b), and adding Claims 49-51. New Claim 49 contained item b) from Claim 1 in dependent form. New Claims 50 and 51 were essentially the same as former Claims 37 and 38, rewritten to depend from new Claim 49.

The AAF received by the USPTO on June 10, 2004 amended the claims as described above, and added Claim 52 which is essentially the same as Claim 40 as originally filed and previously canceled in error. In addition, the AAF included amendments to the Specification to correct typographical and clerical errors in Tables V and VII as originally filed.

The only issue has been obviated by the amendments presented both in draft form to the Examiner prior to the telephonic interview and in the AAF. The claims are presented in the Claims Appendix as they would appear upon entry of the AAF.

No Advisory Action or other communication has been received by Applicants' Attorney from the USPTO despite numerous telephone calls to Examiner Swartz, the Examiner's supervisor, Lynette F. Smith, and to Jasmine Chambers. Applicants' Attorney left voice mail for the Examiner at (571) 272-0865 on August 9 and 10 of 2004. No return telephone call was received from the Examiner. Applicants' Attorney left voice mail for the Examiner on October 18, 2004 and on October 25, the Examiner returned the call and stated that the case had been pulled and would be finished that week. No Advisory Action or other paper has been received from the USPTO to date and there are no entries in PAIR dated after August 30, 2004. On December 20, and 23 Applicants' Attorney left voice mail for the Examiner, but no return telephone call was received from the Examiner. Applicants' Attorney again left voice mail for the Examiner on January 14 and 28 and also left voice mail for Supervisory Examiner Smith on January 21 and 28. No return phone call was received from either the Examiner or the Supervisory Examiner. Applicants' Attorney and Doreen M. Hogle left voice mail for Jasmine Chambers on February 1, 2005. To date, no return telephone call has been received from the Examiner, the Supervisory Examiner, or Ms. Chambers.

V. SUMMARY OF CLAIMED SUBJECT MATTER

The claimed invention is drawn to a composition comprising OspC polypeptides from Lyme Disease causing *Borrelia*.¹ The composition comprises one or more OspC polypeptides from at least two *Borrelia burgdorferi sensu stricto* OspC families selected from the group consisting of: A, B, I, and K, excepting the combination consisting of two OspC proteins wherein one OspC protein is from family A and the second OspC protein is from family I.²

In one embodiment, the composition further comprises at least one OspC polypeptide from each of *Borrelia afzelii* OspC families A and B.³

In another embodiment, the composition comprises a chimeric protein comprising OspC polypeptides from two or more Lyme Disease causing OspC families of Lyme Disease causing *Borrelia* wherein said chimeric protein comprises a first OspC polypeptide encoded by a nucleic acid comprising a sequence from about nucleotide 26 to about nucleotide 621 of an *ospC* gene from a first OspC family, and a second OspC polypeptide encoded by a nucleic acid comprising a sequence from about nucleotide 28 to about nucleotide 570 of an *ospC* gene from a second OspC family, wherein said OspC families are selected from the group consisting of: *Borrelia burgdorferi sensu stricto* OspC families A, B, I, and K, and *Borrelia afzelii* OspC families A and B.⁴ In another embodiment, the composition comprises a chimeric protein comprising OspC polypeptides from two or more Lyme Disease causing OspC families of Lyme Disease causing *Borrelia* wherein said chimeric protein comprises: a first OspC polypeptide encoded by a nucleic acid comprising a sequence from about nucleotide 53 to about nucleotide 570 of an *ospC* gene from a first OspC family and a second OspC polypeptide encoded by a nucleic acid comprising a sequence from about nucleotide 28 to about nucleotide 570 of an *ospC* gene from a second OspC family, wherein said OspC families are selected from the group consisting of: *Borrelia*

¹Specification, page 4, lines 15-16.

²Specification, page 4, lines 16-20.

³Specification, page 22, lines 16-18.

⁴Specification, page 17, lines 1-5.

burgdorferi sensu stricto OspC families A, B, I, and K, and *Borrelia afzelii* OspC families A and B.⁵

In another embodiment, the composition comprises a chimeric OspC protein selected from the group consisting of: SEQ ID NOS: 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, and 84.⁶

VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

Whether the Specification enables the Claims 1-11, 39, 41-43, and 49-52 under 35 U.S.C. § 112, first paragraph, where the claims have been amended to remove the phrase “or immunogenic fragments thereof” and where the Specification demonstrates the efficacy of eight specific examples and provides 32 other specific examples,⁷ and where the art of molecular biology and protein purification is high, such that based on the teachings of the Specification, one of ordinary skill in the art can make and use the claimed compositions with no, or only routine experimentation.

Grouping of Claims

Group I: Claims 1-5 as amended in the AAF, Claims 7-11, and new Claims 49-51 stand or fall together.

Group II: Claim 6 as amended in the AAF, Claims 39, 41, 42, and new Claim 52 stand or fall together.

Group III: Claim 43 stands or falls by itself.

VII. ARGUMENT

The test for enablement is whether the Specification teaches one of ordinary skill in the art how to make and use the claimed invention without undue experimentation.⁸ The claimed

⁵Specification, Claim 41 as originally filed.

⁶Specification, Claim 43 as originally filed.

⁷Specification, page 39, Table V and page 43, Table VII.

⁸*In re Wright*, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. Cir. 1993).

invention is enabled because based on the teachings of the Specification, the well-developed art of molecular biology and protein purification, and the high level of skill in the art, only routine, if any, experimentation is required to make and use the invention commensurate in scope with the claims.

The Examiner stated that the Specification is enabling for protein compositions comprising *B. burgdorferi sensu stricto* OspC proteins LipCB31, LipC12, UnlipC2, UnlipC2C7, UnlipC2C10, UnlipC2C12, UnlipC5C10, and UnlipC5C12,⁹ but that the Specification “does not reasonably provide enablement for compositions comprising OspC from other *Borrelia*, or immunogenic fragments thereof.”¹⁰ In the Office Action made Final, The Examiner stated that he “has considered applicants argument (from the Amendment dated September 6, 2002), but does not find it persuasive for the scope of the instant claims, i.e. any/all immunogenic fragments. . .” (emphasis added)¹¹

Claims 1-6 were amended in the AAF to omit the phrase “immunogenic fragments thereof,” thereby obviating the rejection. Claims 7-11, 39, and 41-43 did not contain the phrase “immunogenic fragments thereof;” therefore, Claims 7-11, 39, and 41-43 are enabled by the Specification without amendment.

The three groups of claims are separately patentable not only because the scope of each group is different, but also because each group is separately enabled by the Specification. Enablement for each group is addressed under separate headings.

Group I: Claims 1-5 and 7-11

The Specification provides enablement for compositions of OspC polypeptides comprising at least two *Borrelia burgdorferi sensu stricto* OspC families selected from the group consisting of A, B, I, and K.¹² The Specification provides enablement for compositions further comprising OspC polypeptides from at least one OspC polypeptide from each of *Borrelia afzelii*

⁹Office Action dated March 26, 2002, page 3, Item 7; and Office Action made Final, dated February 10, 2004, page 2, Item 7.

¹⁰*Id.*

¹¹*Id.*, at page 3, second full paragraph.

¹²Specification, page 14, line 26 through page 15, line 4.

OspC families A and B.¹³ The Specification teaches the general principle that four families of *Borrelia burgdorferi sensu stricto* are responsible for disseminated disease in the human population, as defined by the *ospC* gene.¹⁴ The Specification provides exemplary members for each family and teaches that the *ospC* genes within each family are at least about 98% homologous.¹⁵ In addition, the Specification teaches the general principle that two families of *Borrelia afzelii* are responsible for disseminated disease in the human population, as represented by the *ospC* gene.¹⁶ The Specification provides exemplary members for each of these families and teaches that the genes within each family are at least about 99% homologous.¹⁷

The Specification provides assays to test both the antigenicity¹⁸ and the immunogenicity¹⁹ of the OspC polypeptides of the present invention. The Specification demonstrates the use of both assays for OspC compositions comprising whole OspC, fragments of OspC and chimeric OspC.

As noted by the Examiner, the Specification enables that eight different and specific examples of OspC compositions (LipCB31, LipC12, UnlipC2, UnlipC2C7, UnlipC2C10, Unlip C2C12, UnlipC5C10 and UnlipC5C12).²⁰ According to the Specification, each of the eight examples, without exception, is antigenic and immunogenic, as shown using the assays described in the Specification, demonstrating the predictability of the claimed invention.²¹ Furthermore, the Specification provides additional specific OspC compositions²² and teaches that other members of the four *Borrelia burgdorferi sensu stricto* families or other members of the two

¹³Specification, page 16, lines 4-11, and page 22, lines 16-18.

¹⁴Specification, page 31, line 8, through page 34, line 11.

¹⁵Specification, page 15, line 12, through page 16, line 3, Table II on page 29, and page 31, lines 8-18.

¹⁶Specification, page 34, lines 12-21.

¹⁷*Id.*

¹⁸Specification, page 36, line 5, through page 38, line 15.

¹⁹Specification, page 40, line 6, through page 42, lines 26 and Figures 2-7.

²⁰Office Action dated March 26, 2002, page 3, Item 7; and Office Action made Final, dated February 10, 2004, page 2, Item 7.

²¹Specification, page 36, line 1 through page 40, line 3 and Figure 8; Specification, page 40, line 4 through page 42, line 26

²²Specification, Table VII, page 43.

Borrelia afzelii families can be used in the OspC containing compositions of the present invention.²³

The Examiner has given no reason to doubt the objective evidence of the Specification. The Examiner has indicated that only a subset of the disclosed OspC proteins (LipCB31, LipC12, UnlipC2, UnlipC2C7, UnlipC2C10, Unlip C2C12, UnlipC5C10 and UnlipC5C12) are enabled by the Specification. However, as described above, the Specification has provided a general teaching that four families of *Borrelia burgdorferi sensu stricto* and two families of *Borrelia afzelii* are responsible for disseminated human disease and that the *OspC* genes of the members of a given family are 98% and 99% homologous, respectively. The Specification provides eight examples of OspC containing compositions, including whole OspC (LipCB31 and LipC12) and unlipidated OspC (UnlipC2), each of which were demonstrated to be both antigenic and immunogenic. Given the proven examples and the well-defined families of *Borrelia burgdorferi sensu stricto* and *Borrelia afzelii*, and the assays for antigenicity and immunogenicity provided in the Specification, one of ordinary skill in the art can make and use the invention commensurate in scope with the claims without undue experimentation. Withdrawal and reconsideration of the rejection are respectfully requested.

Group II: Claims 6 and 39, 41, 42, and new Claim 52

The chimeric proteins of Claims 6 and 39, 41, 42, and 52 are enabled because based on the teachings provided in the Specification, one of ordinary skill in the art would know how and be able to produce the chimeric OspC of the present invention without undue experimentation. The Specification provides the sequences of both lipidated and unlipidated OspC²⁴ and teaches that at least 22 *ospC* sequences are available in GenBank. The Specification teaches chimeric OspC proteins comprising two or more polypeptides as claimed.²⁵ According to the Specification, the nucleotide numbering is based on the OspC sequence from B31, as numbered

²³Specification, page 15, line 12, through page 16, line 12.

²⁴Specification, see for example, Table V, page 3.

²⁵Specification, see page 17, lines 1-25; and page 36, line 1 through page 44, line 2.

in GenBank accession number U01894, wherein base one is in the start codon.²⁶ The Specification provides the DNA and protein sequences of several OspC chimeric proteins as presently claimed.²⁷ Using the teachings of the present invention regarding which OspC family members and which portion of said OspC family members to use, one of ordinary skill in the art can make and use the OspC chimeras of the present invention using no more than routine molecular biology techniques. Withdrawal and reconsideration of the rejection are respectfully requested.

Group IV: Claim 43

Claim 43 is drawn to specific OspC proteins selected from the indicated SEQ ID NOS. As noted by the Examiner, the Specification is enabled for several compositions including five chimeric OspC polypeptides (UnlipC2C7 (SEQ ID NO: 32), UnlipC2C10 (SEQ ID NO: 34), Unlip C2C12 (SEQ ID NO: 36), UnlipC5C10 (SEQ ID NO: 40) and UnlipC5C12 (SEQ ID NO: 42)). As described above, all of the chimeric OspC tested were antigenic and immunogenic, demonstrating the predictability of the claimed invention. Therefore, based on the Specification and the working examples, one of ordinary skill in the art can make and use the chimeric OspC proteins of Claim 43 with a reasonable expectation of success and without undue experimentation. Withdrawal and reconsideration of the rejection are respectfully requested.

²⁶Specification, page 25, lines 21-23.

²⁷Specification, see for example, Table V, page 39.

VIII. CONCLUSION

The claimed invention is enabled because based on the teachings of the Specification, the well-developed art of molecular biology and protein purification, and the high level of skill in the art, only routine, if any, experimentation is required to make and use the invention commensurate in scope with the claims.

Respectfully submitted,

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CLAIMS APPENDIX**Claim Listing**

1. A composition comprising OspC polypeptides from Lyme Disease causing *Borrelia* wherein said composition comprises one or more OspC polypeptides from at least two *Borrelia burgdorferi sensu stricto* OspC families selected from the group consisting of: A, B, I, and K, excepting the combination consisting of two OspC proteins wherein one OspC protein is from family A and the second OspC protein is from family I.
2. The composition of Claim 1 comprising one or more OspC polypeptides from each of said *Borrelia burgdorferi sensu stricto* families.
3. The composition of Claim 1, wherein said OspC polypeptide comprises the OspC protein variable region.
4. The composition of Claim 3, wherein said OspC polypeptide is encoded by a nucleic acid comprising nucleotide 26 to about nucleotide 621 of an *ospC* gene.
5. The composition of Claim 3, wherein said OspC polypeptide is encoded by a nucleic acid comprising nucleotide 53 to about nucleotide 570 of an *ospC* gene.
6. The composition of Claim 1, wherein at least two of said OspC polypeptides are fused together in a single protein, encoded by a single nucleic acid, wherein polypeptides in said fusion protein are not found in the same configuration in a naturally occurring OspC protein.
7. The composition of Claim 1, wherein the *ospC* genes encoding the OspC polypeptides within a given OspC family are at least 98% identical at the nucleic acid level.

8. The composition of Claim 7, wherein *Borrelia burgdorferi sensu stricto* OspC family A comprises strains B31, CA4, HII, IPI, IP2, IP3, L5, PIF, Pka, Txgw and strains containing *ospC* allele OC1.
 9. The composition of Claim 7, wherein *Borrelia burgdorferi sensu stricto* OspC family B comprises strains 35B808, 61 BV3, BUR, DK7, PB3, Z57 and strains containing *ospC* genes OC2 and OC3.
 10. The composition of Claim 7, wherein *Borrelia burgdorferi sensu stricto* OspC family I comprises strains 297, HB19 and strains containing *ospC* gene OC10, wherein strain 297 is characterized by *ospC* of GenBank accession number L42893.
 11. The composition of Claim 7, wherein *Borrelia burgdorferi sensu stricto* OspC family K comprises strains 272, 297, 28354, KIPP, MUL and strains containing *ospC* gene OC12 and OC13, wherein strain 297 is characterized by *ospC* of GenBank accession number U08284.
39. A chimeric protein comprising OspC polypeptides from two or more Lyme Disease causing OspC families of Lyme Disease causing *Borrelia* wherein said chimeric protein comprises:
- a) a first OspC polypeptide encoded by a nucleic acid comprising a sequence from about nucleotide 26 to about nucleotide 621 of an *ospC* gene from a first OspC family and
 - b) a second OspC polypeptide encoded by a nucleic acid comprising a sequence from about nucleotide 28 to about nucleotide 570 of an *ospC* gene from a second OspC family,
- wherein said OspC families are selected from the group consisting of: *Borrelia burgdorferi sensu stricto* OspC families A, B, I, and K, and *Borrelia afzelii* OspC families A and B.

41. A chimeric protein comprising OspC polypeptides from two or more Lyme Disease causing OspC families of Lyme Disease causing *Borrelia* wherein said chimeric protein comprises:
 - a) a first OspC polypeptide encoded by a nucleic acid comprising a sequence from about nucleotide 53 to about nucleotide 570 of an *ospC* gene from a first OspC family and
 - b) a second OspC polypeptide encoded by a nucleic acid comprising a sequence from about nucleotide 28 to about nucleotide 570 of an *ospC* gene from a second OspC family,wherein said OspC families are selected from the group consisting of: *Borrelia burgdorferi sensu stricto* OspC families A, B, I, and K, and *Borrelia afzelii* OspC families A and B.
42. The chimeric protein of Claim 41, wherein said protein is unlipidated.
43. A chimeric OspC protein selected from the group consisting of: SEQ Id Nos: 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, and 84.
49. The composition of Claim 1, further comprising at least one OspC polypeptide from each of *Borrelia afzelii* OspC families A and B.
50. The composition of Claim 49, wherein *Borrelia afzelii* OspC family A comprises strains Pbo, Pwud, PKO, Pgau, DK2, DK3, DK21, DK8, Bfox and JSB.
51. The composition of Claim 49, wherein *Borrelia afzelii* OspC family B comprises strains DK5, ACA1, DK9, XB18h, Ple and 134M.
52. The chimeric protein of Claim 39, wherein said protein is unlipidated.